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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/774,490	01/31/2001	Shengfang Jin	07334-138001	3043

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1642	10

DATE MAILED: 05/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/774,490	Jin
Examiner	**Art Unit**
Karen Canella	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____ .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above, claim(s) *5-22* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 7
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Acknowledgment is made of applicant's election, without traverse, of Group I, drawn to methods for determining whether a test compound modulates the drug resistance of a cell.

2. Claims 1-22 are pending. Claims 5-22, drawn to non-elected invention, are withdrawn from consideration. Claims 1-4 are examined on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for eukaryotic cells and known proteins and nucleic acid sequences encoding said proteins which modulate drug resistance in human cells, does not reasonably provide enablement for prokaryotic cells or mouse proteins obtained from the transplanted fibrosarcoma model and nucleic acid sequences encoding said proteins which do not have a known human homolog. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification teaches that semaphorin D and 24p3 are proteins which are differentially expressed in a drug-resistant EMT-6 cell line. The EMT-6 cell line is a mouse mammary sarcoma. The specification provides no teachings as to the corresponding human proteins of semaphorin D or 24p3, nor does it teach human tissues or tumors wherein the claimed semaphorin D or 24p3 sequences or human homologs thereof would be expected to be upregulated in response to drugs. It is known in the art that the EMT-6 cell line ~~does~~ has an RNA expression profile that is not anticipatory with respect to other cell lines, such as RIF-1 lines (British Journal of Cancer, 1992, vol. 65, pp. 239-245), therefore it cannot be assumed that genes

overexpressed in drug resistant EMT-6 will also be overexpresed in human drug resistant cells. Further, the scope of the claims should be commensurate with the scope of the teachings of the specification and the specification does not teach methods for assessing the effect of a test compound on drug resistance sequences in procaryotic cells. Due to this lack of guidance on the exact human sequences of semaphorin D or 24p3, and lack of teaching on where to find the human homologs of semaphorin d or 24p3, one of skill in the art would be subject to undue experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 1 and 4 are rejected under 35 U.S.C. 102(e) as being anticipated by Shyjan et al (USP 5,932,422). Claim 1 is drawn in part to a method for determining whether a test compound modulates the drug resistance of a cell comprising determining the level of expression or activity of a resistance sequence in a cell in the presence of a test compound, determining the level of expression or activity of a resistance sequence in a cell in the absence of a test compound, and identifying a compound as a modulator of drug resistance if the level of expression or activity of the resistance sequence in the presence of the test compound differs from the level of expression or activity in the absence of the test compound. Claim 4 is drawn to a resistance sequence encoded by an endogenous gene. Shyjan et al disclose a method of identifying a compound that modulates drug resistance, the method comprising determining the level of expression or activity of ubiquitin carboxy-terminal hydrolase in a cell in the presence of a test compound; determining the level of expression or activity of ubiquitin carboxy-terminal hydrolase in a cell in the absence of a test compound; identifying said compound as a modulator of drug resistance when the level of expression or activity of ubiquitin carboxy-terminal hydrolase is decreased in the presence of said compound (claim 4 and claim 13 of Shyjan et al). Shyjan et al disclose ubiquitin carboxy-terminal hydrolase as an endogenous gene (column 11, lines 42-44).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nilsen-Hamilton et al (Gene, 1987, vol. 51, pp. 163-170) in view of Stein et al (Proc Am Assoc Cancer Res, 1997, Vol. 38, page A3215). The embodiments of claims 1 and 4 are listed above. Claim 3

specifically embodies nucleic acids semaphorin D, B94, mel-14 antigen, 24p3, proliferin and maspin as resistance sequences. Claim 4 specifically embodies the polypeptides of semaphorin D, B94, mel-14 antigen, 24p3, proliferin and maspin as resistance sequences.

Nilsen-Hamilton et al teach the multidrug resistance-associated protein, MRP, as the human homolog of mouse proliferin.

Stein et al teach the modulation of MRP expression and activity levels by TNF-alpha, thus Stein et al teaches a method for determining whether the test compound of TNF-alpha modulates the expression and activity of MRP in a cell.

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to measure the modulation of the expression or activity of proliferin in the presence or absence of a test compound. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Nilsen-Hamilton et al on the homology between the proliferin gene and the MRP gene.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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May 6, 2002

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